REMARKS

Claims 44-70 were previously pending. Applicants appreciate the Examiner's withdrawal of the rejections of claims 51-59 and 70 under 35 USC §§ 112, 102(b) and 103(a). With this paper, claims 51, 52 and 70 have been amended and new claims 71-73 are presented. Applicants respond to the Office Action as follows. A Request for Continued Examination is being filed herewith. Also enclosed is a Declaration under 37 CRF 1.132 and selected references discussed in the Declaration.

Rejections under 35 USC § 112

All the pending, non-newly presented and non-withdrawn claims stand rejected based on the contention that they fail to comply with the written description and enablement requirements. For at least the following reasons, Applicants respectfully request the Examiner to reconsider and withdraw the stated rejections.

At the outset, Applicants disagree that the previously pending claims would be viewed as not adequately described or enabled by one skilled in the art at the time the instant application was filed. Nevertheless, in order to expedite allowance of the present application, claim 51 has been amended to specify that the OMVs are from N. meningitidis, N. gonorrhoeae or N. lactamica. Basis for this amendment can be found at least on page 5, lines 4-8; page 8, lines 27-31; page 11, lines 10-11; and page 12, lines 12-20. Claim 51 has been further amended to recite that the OMVs have a reduced content of Neisseria Opa that binds to human CEACAM1. Basis for this amendment can be found throughout the specification as filed, and for instance, at least on page 4, lines 15-19; page 5, lines 20-21 and page 10, lines 31-32The enclosed Declaration of Dr. Andrew Gorringe (an inventor on the present application and expert in the art, as evidenced by his included Curriculum Vitae) also details numerous passages in the description that provide an enabling and adequate written description of the OMVs recited in the pending claims.

Applicants also present herewith new independent claims 71 -73. Basis for the new claims can be found at least on page 4, lines 15-19; page 5, lines 20-21; page 8, lines 13-17; and

page 10, lines 31-32. The Examiner is respectfully requested to enter and examine the new claims.

With the claim amendments presented herein, Applicants submit that the contentions in the Office Action that the specification does not make *Neisseria* that is "free" of Opa is rendered moot. Further, the contention that the recited genus includes outer membrane preparations from all Neisserial species has been rendered moot. In particular, as noted above, claim 51 is now limited to *N. meningitidis, N. gonorrhoeae* and *N. lactamica*. Applicants further submit that the contention in the Office Action that there are "vast" Opa loci has also been rendered moot, since the number of Opa loci has been limited with the amendments presented herewith. Moreover, the enclosed Delcaration of Dr. Gorringe corroborates the specification as filed in that one skilled in the art would not consider the total number of Neisseria Opa loci to be "vast", particularly in view of the amendment to the claims such that they are limited to the three aforementioned Neisserial species.

With respect to the contention in the Office Action that the Examples and Figures in the specification as filed do not demonstrate a Neisseria outer membrane preparation that is free of Opa that binds human CEACAM-1, Applicants reiterate that the claims have been amended to eliminate the term "free" of, and further respectfully point out it is well known in the art that *Neisseria* are obligate human pathogens. Thus, the clinically relevant binding interaction is between *Neisseria* Opa and human CEACAM1. Applicants further submit it is well known in the art that human CEACAM1 is found on the surface of human T cells. As described in the present application, binding of *Neisseria* OMVs containing hCEACAM1-reactive Opa protein to T cells (via hCEACAM1) suppresses proliferation and activation of the T cells. This immunosuppressive effect therefore reduces efficacy of previously available Neisserial OMVs as vaccines. Further, the present specification on page 11, lines 29-35, discloses that previously available formulations against Neisserial disease induce these undesirable immunosuppressive effects via binding to hCEACAM1 on the surface of human T cells. Applicants submit it is this problem that the present invention solves. Moreover, in contrast to the position adopted in the Office Action, and as discussed on page 12, lines 5-8 of the present application, Neisseria Opa proteins do not recognize murine or other

CEACAM1 proteins, and thus the animal models typically used to assess vaccine efficacy do not illustrate the immunosuppressive effect. Accordingly, the Examples of the present specification employ human CEACAM1, such as that expressed by the human T cells described in Example 1 (Jurkat cells). In pointing out these features of the application as filed, Applicants do not rely on arguments of counsel alone, and in connection with this, the Examiner's attention is respectfully directed to the enclosed declaration of Dr. Gorringe, which details the interpretation of the application as filed as viewed by one skilled in the art. To summarize, and as Dr. Gorringe declares, the results presented in the application demonstrate that OMVs containing hCEACAM1-reactive Opa bind hCEACAM1 and have immunosuppressive effects on human T cells. However, these undesirable effects are reduced via performance of the present invention, which entails use of OMVs that have a reduced content of hCEACAM1-reactive Opa. In particular, and as also detailed in the Declaration of Dr. Gorringe, the specification as filed demonstrates not only the production of *Neisseria* OMVs that have a reduced content of hCEACAM1-reactive Opa protein, but further demonstrates that these OMVs exhibit improved properties as compared with "normal" OMVs containing hCEACAM1-reactive Opa protein. Applicants courteously but vehemently point out that the Examiner is incorrect in the contentions set forth in the Office Action regarding Figure 2. In connection with this, Applicants point out that Figure 2A illustrates that Opa protein was not detected in OMVs from the Opa –ve strain or in OMVs from N. lactamica. Thus, and as corrobrated in Dr. Gorringe's declaration, the results illustrated for the Opa –ve OMVs represent the background signal, and are within the confidence intervals of the negative controls.

With respect to the contention in the Office Action that it would be far outside the realm routine experimentation to practice the invention, Applicants respectfully disagree. In particular, Applicants reiterate that the present claims have been amended to recite only three Neisseiral strains. Furthermore, the entire *N. meningitidis* and *N. gonorrhoeae* genome sequences were publically available before the filing date of the present application. Further still, Dr. Gorringe's Declaration corroborates the specification as filed insofar as one skilled in the art would indeed be able to use well known genetic engineering techniques to make OMVs which have a reduced content of hCEACAM1-reactive Opa, as recited in the present claims. Thus, Applicants respectfully submit it is clear from the remarks, amendments, and supportive documentation

provided herewith that one skilled in the art would conclude that the now pending claims are supported by an adequate written description and are fully enabled by the specification as filed. The Examiner is therefore respectfully requested to reconsider and remove the stated rejections.

Conclusion

In view of the foregoing amendments and remarks, Applicants believe all of the pending, non-withdrawn claims are now in condition for allowance and respectfully request the Examiner to reconsider the rejections and allow all of the claims. A Request for Continued Examination is included herewith. Applicants request a one-month extension of time to file this response, and any other extension of time that is necessary to file any paper during prosecution of this application. Fees due for this and any other submission during prosecution of this application can be charged to Deposit Account No. 08-2442.

Respectfully submitted,

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